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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,046	02/20/2002	Jim Wells	SUNESIS.2DV1C2	9481

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EXAMINER	
EPPERSON, JON D	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/082,046	Applicant(s) WELLS ET AL.	
File Copy	Examiner Jon D Epperson	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-63* is/are pending in the application.

4a) Of the above claim(s) *44 and 52-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-43 and 45-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Please note: The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to **Group Art Unit 1639**.

Status of the Application

1. Receipt is acknowledged of a Response to Restriction Requirement, which was dated on September 24, 2002 (Paper No. 4).

Priority Claims

2. The effective filing date of the claims is the filing date of the case i.e., February 20, 2002 (see New Matter Rejection below).

Status of the Claims

3. Claims 40-63 are pending in the present application in accordance with applicants transmittal sheet and the Preliminary Amendment dated February 20, 2002. The Examiner thanks applicants for bringing this matter to his attention. Consequently, the previous Restriction Requirement is withdrawn with the EXCEPTION of the Species Election.

4. Please note: Please note that applicants' elected species (see Response to Restriction Requirement, Paper No. 14) were found in the art, see rejections below. Applicant is reminded of MPEP § 803.02 with respect to species elections:

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

5. Claims 44 and 52-63 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species, the requirement having been traversed in Paper No. 14 (see below i.e., ***Response to Restriction and/or Election of Species***).

6. Therefore, claims 40-43 and 45-51 are examined on the merits in this action.

Response to Restriction and Election of Species

7. Applicant's election of Species in Paper No. 14 with traverse is acknowledged. The Examiner thanks applicants for making a proper response to the Restriction Requirement with regard to "includ[ing] an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added" as outlined in paragraph 15 of the Restriction Requirement (see Paper No. 3) in light of

potentially confusing language as outlined by applicants (see Paper No. 14, page 2, paragraphs 1-2).

8. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a)).

9. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

10. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

11. The references listed on applicant's PTO-1449 form have been considered by the examiner. A copy of the form is attached to this Office Action.

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 40-43 and 45-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (NEW MATTER). Claim(s) 40-43 and 45-51 were added in the Preliminary Amendment dated February 20, 2002. However, applicant did not show where support for these addition(s) could be found in the specification. Applicant is required to disclose where in the specification support for the amendment(s) and/or new claims is located. If applicant believes this rejection is in error, applicant must disclose where in the specification support for new claims 40-43 and 45-51 can be found. As a result, claim 40-43 and 45-51 represent new matter. Please note that an amendment filed along with the filing of an application (as in the present Preliminary Amendment) does not enjoy the status as part of the original disclosure in an application filed under 37 CFR 1.53(b) unless it is specifically referred to in the oath or declaration filed therewith (e.g., see MPEP 608.04b). In the present instance, the oath or declaration fails to specifically refer to the Preliminary Amendment in its "reviewed and understands" clause (which is lacking); nor does the present declaration indicate that a CIP was intended to be filed by applicant.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 40-43 and 45-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Erlanson et al (Erlanson, D. A.; Braisted, A. C.; Raphael, D. R.; Randal, M.; Stroud, R. M.; Gordon, E. M.; Wells, J. A. "Site-directed ligand discovery" *PNAS* **August 15, 2000**, *97(17)*, 9367-9372).

For ***claim 40***, Earlanson et al discloses a method called "tethering" to "discover low molecular weight ligands (~250 Da) that bind weakly to targeted sites on proteins through an intermediary disulfide tether", which anticipates the preamble of claim 40. Erlanson et al discloses a "(a) containing a target protein comprising a –SH group" (see Erlanson et al, page 9367, entire document, especially figure 1, showing SH group on protein and last paragraph of column 40 showing use of thymidylate synthase enzyme), which anticipates claim 40 (a). Erlanson et al discloses "(b) combining said target protein with one or more ligand candidates wherein said ligand candidates each comprises a disulfide bond, and wherein said ligand candidates are not peptides and are ach less than about 2000 daltons in size (see Erlanson et al, entire document, especially figure 1, showing multiple ligands with disulfide bonds i.e., represented as different

shapes; see also disulfide libraries section, second paragraph, "Libraries (not shown) were also constructed from mono-BOC-protected cystamine and a variety of sulfonyl chlorides, isocyanates and thiocyanates ... Finally, oxime-based libraries were constructed ...") (see also abstract, "We report a strategy (calletd "tethering") to discover low molecular weight ligands (~250 Da) that bind weakly to targeted siteson proteins through an intermediary disulfide tether"), which anticipates claim 40 (b). Erlanson et al discloses "forming a taget protein-ligand conjugate wherein at least one ligand candidate binds to the target protein and forms a disulfide bond with the target protein under disulfide exchange conditions" (see Erlanson et al, entire document, especially figure 1, showing formation of disulfide bond; see also disulfide library screening section, paragraph 40, "The reaction is done in a buffer containing 25 mM postassium phosphate (pH 7.5) and 40 mM 2-mercaptoethanol"), which anticipated claim 40(c). Finally Erlanson et al discloses "detecting the formation of said protein-ligand conjugate and identifying he ligand present is said conjugate (see Erlanson et al, entire document, especially figure 2).

For ***claims 41-43***, Erlanson et al discloses ligands that are ~ 250 daltons (see Erlanson et al, abstract), which anticipates claims 41-43.

For ***claims 45-47***, Erlanson et al discloses the use of 2-mercaptoethanol (see Erlanson et al, page 9368, column 2, "disulfide library screening" section), which anticipates claims 45-47.

For ***claims 48-51***, Erlanson et al discloses the use of mass spectrometry to detect the protein-ligand conjugate both with and without fragmentation to identify said ligand

(see Erlanson et al, entire document, especially page 9369, Results and Discussion Section; see also figure 2), which anticipates claims 48-51.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 40-43 and 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paalman et al (Paalman, S. R.; Noll, D. M.; Clarke N. D. "Formation of a covalent complex betwenn methylguanine methyltransferase and DNA via disulfide bond formation between the active site cysteine and a thiol-containing analog of guanine" *Nucleic Acids Research* **1997**,

25(9), 1795-1801) and Liem et al (Liem, L. –K; Wong, C. –W.; Lim, A.; Li, B. F. L. "Factors Influencing the Repair of the Mutagenic Lestion O6-methylguanine in DNA by Human O6-methyl guanine-DNA Methyltransferase" *J. Mol. Biol.* **1993**, 231, 950-959).

For ***claim 40***, Paalman et al teaches a method for "identifying" a DNA "non-peptide" ligand that bind to a methylguanine methyltransferase "target protein" (see Paalman et al, page 1795, abstract). Furthermore, Paalman et al teaches that said "target protein" contains five cysteines (i.e., -SH groups) and only one of them is "activated" (see Paalman et al, page 1815, conclusion, first paragraph) ("Methylation of this single cysteine appears to abolish the ability to form an SDS-resistant complex despite the existence of four other cysteines in the protein. We interpret this to mean that the active site cysteine is the predominant, if not exclusive, residue with which the oligonucleotide forms a stable disulfide bond. This specificity is especially remarkable given that the active site residue is substantially buried in the crystal structure of *E. coli* Ada (and presumably in the homologous human protein used in these experiments"). In addition, the methylguanine methyltransferase "target protein" is combined with more than one DNA sequence "ligand" that contains a base modified with a disulfide bond, 2'-deoxy-6-(cystamine)-2-aminopurine (d^6Cys^2-AP) nucleoside (see Paalman et al, page 1811, figure 2 and page 1813, "Sequences" section). Furthermore, the sequences containing the d^6Cys^2-AP substitution bind to the "target protein" under reducing conditions via the formation of a disulfide bond (see Paalman et al, page 1814, column 2, paragraphs 1 and 2) ("Human MTase was incubated with radiolabeled oligonucleotide containing the

reduced d^6Cys^2AP-derived nucleoside ... These results suggest that the complex is formed via a disulfide bond"). Finally, the "target protein-ligand" complex was identified including the exact position wherein said "ligand" binds to said "target protein" via purificiation of the biotinylated DNA on avidin-coated beads (see Paalman et al, page 1815, column 1, paragraph 1) ("The complex was then digested overnight with trypsin. Peptides that remained bound to the DNA was purified by binding to biotinylated DNA to avidin-coated beads and collecting the beads by centrifugation").

For ***claims 45-46***, Paalman et al teaches forming complex between the methylguanine methyltransferase "target protein" and the d^6Cys^2-AP substituted DNA "ligand" under reducing conditions i.e., using DTT (see Paalman et al, page 1814-15, figures 3-4).

The prior art teachings of Paalman et al differ from the claimed invention as follows:

For **claims 40-43**, Paalman et al is deficient in that it does not specifically teach a "ligand" that is less than about "2000", "1500", or "750" daltons in size (the d^6Cys^2-AP substituted DNA "ligands" are ~6,000 daltons for each strand, see Paalman et al, page 1813, "Sequences" section).

For **claims 47**, Paalman et al is deficient in that although it teaches the use of DTT as a reducing agent, it does not specifically teach the use of 2-mercaptoethanol as the reducing agent. However, any reducing agent commonly used would have been obvious including 2-mercaptoethanol because each would have the same effect and the final decision would ordinarily be determined on cost and availability of the reagents.

However, Liem et al teaches the following:

For **claims 40-43**, Liem et al teaches that the methylguanine methyltransferase "target protein" can bind to "smaller" target DNA ligands including a "library" of dinucleotides (MW ~660), which would have a molecular weight less than "2000", "1500" or "750" Daltons (see Liem et al, page 955, Table 3). The DNA ligands were "detected" using HPLC equipped with an autosampler linked directly to a radioactive flow detector (see Liem et al, page 952, Experimental conditions).

It would have been obvious to one skilled in the art at the time the invention was made to "identify" a DNA "ligand" that binds to a methylguanine methyltransferase "target protein" wherein said DNA "ligand" possesses a disulfide bond (i.e., contains d^6Cys^2AP) and binds to said "target protein" under reducing conditions as taught by Paalman et al, with DNA "ligands" that are less than 750 daltons as taught by Liem et al because Liem et al "explicitly" states that dinucleotides (MW ~660 daltons) can bind to the same "target protein" (see Liem et al, page 955, Table 3) and Paalman et al explicitly teaches a "general" method for incorporating d^6Cys^2AP into DNA using an Applied Biosystems model 392 DNA synthesizer using standard phosphoramidite chemistry, which would encompass a method for incorporating the d^6Cys^2AP into a DNA "ligand" of any size including the dinucleotides because the method adds nucleotides "one at a time." Furthermore, one of ordinary skill in the art would have been motivated to use the method as taught by Paalman et al with the smaller dinucleotides as taught by Liem et al because according to Paalman et al the d^6Cys^2AP "analog[s] might prove useful for structural studies" (see Liem et al, page 1801, last paragraph), and the smaller

dinucleotide ligands could be used for characterizing the "structural basis" for the "stacking" effect noted by Liem et al (see Liem et al, page 955, Table 3).

17. Claims 40-43 and 45-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paalman et al (Paalman, S. R.; Noll, D. M.; Clarke N. D. "Formation of a covalent complex betwenn methylguanine methyltransferase and DNA via disulfide bond formation between the active site cysteine and a thiol-containing analog of guanine" *Nucleic Acids Research* **1997**, *25(9)*, 1795-1801) and Liem et al (Liem, L. –K; Wong, C. –W.; Lim, A.; Li, B. F. L. "Factors Influencing the Repair of the Mutagenic Lestion O6-methylguanine in DNA by Human O6-methyl guanine-DNA Methyltransferase" *J. Mol. Biol.* **1993**, 231, 950-959) and Ganem et al (Ganem, B.; Li, Y. T.; Henion, J. D. "Detection of noncovalent receptor-ligand complexes by mass spectrometry" *Journal of the American Chemical Society* **1991**, 113(16), 6294-6).

For **claims 40-43 and 45-47**, the combined teachings of Paalman et al and Liem et al teach all the limitations stated in the 35 U.S.C. 103(a) rejection above (incorporated in its entirety herein by reference), which renders obvious claims 40-43 and 45-47.

The prior art teachings of Paalman et al combined with Liem et al differ from the claimed invention as follows:

For **claims 48-51**, the combined teachings of Paalman et al and Liem et al is deficient in that it does not specifically teach a the use of "mass spectrometry" for detecting the protein-ligand complex.

However, Ganem et al teaches the following:

For **claims 48-51**, Ganem et al teaches the use of mass spectroscopy for "identifying enzyme-substrate, receptor-ligand ... complexes" (see Ganem et al, page 6294, paragraph 1), which reads on claim 48. Furthermore, Ganem et al teaches identifying new signals for "[b]inding of FKBP with RM ... giving rise to signals at m/z 1821.3 and 2124.4 for the (FKBP + RM _ NH_4 + 6 H)$^{7+}$ and (FKBP + RM + NH_4 + 5 H)$^{6+}$ charge states, respectively, of the receptor-ligand complex" (see Ganem et al, page 6295, second column, last paragraph), which reads on claim 49 wherein the protein-ligand complex is subjected "directly" to mass spectrometry analysis. In addition, "fragmentation" of the protein-ligand conjugate is also NOT ruled out and, as a result, Ganem et al teaches "fragmentation" (see Ganem et al, page 6294, paragraph 3, "fragementation is usually not observed"). Finally, Ganem et al teaches that the ligand can be "identified" using mass spectrometry (see Ganem et al, page 6296, "This result indicates that noncovalently bound species can be detected directly in a complex mixture without chromatographic separation").

It would have been obvious to one skilled in the art at the time the invention was made to "identify" a "ligand" that binds to a "target protein" wherein said "ligand" possesses a disulfide bond and binds to said "target protein" under reducing conditions wherein said ligand is less than 750 daltons as taught by the combined teachings of Paalman et al and Liem et al in conjunction with the mass spectrometer techniques as taught by Ganem et al because Ganem et al explicitly states that the mass spectrometry "can be applied to problems of biological interest [including] ... proteins" and that the methods are good for "detecting and identifying enzyme-substrate, receptor-ligand

[complexes]" (see Ganem et al, page 6294, paragraph 1), which would encompass the methods of Paalman et al and Liem et al. Furthermore, one of ordinary skill in the art would have been motivated to use the mass spectrometers as taught by Ganem et al with the ligand-receptors as taught by the combined teachings of Paalman et al and Liem et al because Ganem et al explicitly states that the "ion-spray MS can be performed in water without cosolvent, which is ideal for most biological systems. Multiple charging produces a family of molecular ions and dramatically reduces the mass-to-charge ratio so that even quadrupole mass spectrometers having a typical range of 1000-2000 daltons (DA) can determine high MW species with unit mass resolution"(see Ganem et al, page 6294, second paragraph) (see also Ganem et al, page 6296, last paragraph).

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

19. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 40-43 and 45-47 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,335,155 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the referenced patent are essentially drawn to same method of identifying a ligand. For example, both references recite methods for identifying a "ligand" that binds to a "target" wherein said "target" is a protein (see preamble of claim 40 in present application; see also claim 4 of U.S. Pat. No. 6,335,155). Both references recite methods wherein the "ligand" is less than 500 daltons (see claim 44 of present application; see also preamble of U.S. Pat. No. 6,335,155). Both references claim "ligands" that would overlap in scope i.e., contain some of the same members (see claim 1 of present application wherein "ligand is not a peptide and is less than about 2000 daltons in size"; see also claim 1 of U.S. Pat. No. wherein the "ligand is less than 500 daltons in size", which would overlap because a non-peptide ligand that is less than 500 daltons in size would fit into both categories e.g., thioglycerol/thionitrobenzoic acid mixed disulfide). Furthermore, both methods claim reacting said "target" with said "ligand" under "reducing conditions" and further specify using "2-mercaptoethanol" (see claim 47 of the present

application; see also claim 3 of U.S. Pat. No. 6,335,155). Finally, both methods claim subjecting the "target-ligand" complex to mass spectrometry analysis (see claims 48-51 of the present application; see also claim 1 (c) of U.S. Pat. No. 6,335,155). Accordingly it is deemed that the inventions claimed herein and that of the patent are obvious variants of each other.

Status of Claims/Conclusion

21. No claims are allowed.

22. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (703) 308-2423. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

24. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

25. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-2439.

Jon D. Epperson, Ph.D.
November 18, 2002

BENNETT CELSA
PRIMARY EXAMINER